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PRE-APPEAL BRIEF REQUEST FOR REVIEW	Docket Number (Optional) ALEX-P01-112

	Application Number	Filed
	10/583,056	March 16, 2007
	First Named Inventor: Bowdish et al.	
	Art Unit: 1644	Examiner: G. R. Ewoldt

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant /inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [x] attorney or agent of record. Registration number 61,156
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. _____

/Ryan Murphey/
Signature

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Typed or printed name

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Telephone number

June 17, 2010
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

[x] *Total of 1 forms are submitted.

Docket No.: ALEX-P01-112
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Bowdish et al.

Application No.: 10/583,056 Confirmation No.: 8249

Filed: March 16, 2007 Art Unit: 1644

For: NOVEL ANTI-DC-SIGN ANTIBODIES Examiner: G. R. Ewoldt

REMARKS ACCOMPANYING PRE-APPEAL BRIEF REQUEST FOR REVIEW

MS AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to the Final Office Action dated February 23, 2010 and the Advisory Action dated May 4, 2010, Applicants hereby request a Pre-Appeal Brief Review. A request for a one-month extension of time and appropriate fee are submitted concurrently herewith. Please consider the remarks below which accompany Request form PTO/SB/33, filed herewith.

Claims 1-4, 7-9, 13, 19, 20, 31, 32, 48 and 50-52 are rejected under 35 U.S.C. 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleges that the specification and claims as originally filed do not provide support for an antibody defined by the CDRs of SEQ ID NOs: 10 and 45 (light chain) and SEQ ID NOs: 18 and 49 (heavy chain). The Examiner states that this rejection is a "written description rejection for the introduction of new matter into the claims." See Final Office Action at page 2, paragraph 6. Applicants respectfully traverse.

The instant claims are directed to an antibody comprising all six complementarity determining regions (CDRs) of antibody 1G4. As set forth below, Applicants submit that the application clearly provides support for these claims. In particular, the application supports claims to antibodies identified by CDRs and discloses the sequence of all six CDRs of antibody 1G4. Accordingly, the written description/new matter rejection should be withdrawn. As reference for the following discussion, the following Table will be helpful.

SEQ ID NO	Description
10	Complete light chain variable region (frameworks plus CDRs) of antibody 1G4
18	Complete heavy chain variable region (frameworks plus CDRs) of antibody 1G4
45	Light chain CDR3 of antibody 1G4
49	Heavy chain CDR3 of antibody 1G4

Applicants assert that the instant specification clearly supports antibodies claimed by reference to their CDR regions. For example, at paragraph [0038] the specification states,

> "In one embodiment, the antibody includes one **or more** CDR domains of the antibody. In another embodiment, the antibodies utilized in the present disclosure are humanized antibodies having a light chain variable region comprising at least one CDR selected from the group consisting of amino acid sequences of SEQ ID NO:45 ... In yet another embodiment, the antibodies utilized in the present disclosure are humanized antibodies having a heavy chain variable region comprising at least one CDR selected from the group consisting of amino acid sequences of SEQ ID NO: ... 49 ..." (Emphasis added).

Accordingly, the specification clearly indicates that an antibody may include one **or more** CDR domains of the antibody. The specification also makes references to antibodies comprising certain CDR regions, including the heavy chain CDR3 from antibody 1G4 (SEQ ID NO: 49) and the light chain CDR3 of antibody 1G4 (SEQ ID NO: 45). The specification also provides the full heavy and light chain variable region sequences for a variety of antibodies, and calls out all six CDR regions for these sequences (see Figure 4c). The specification also clearly contemplates humanized

antibodies in which the CDRs of mouse monoclonal antibodies, such as 1G4, are inserted into a human immunoglobulin framework (see e.g., paragraph [0037] of US 2008/0025913). Accordingly, the application clearly supports claims to antibodies by reference to their CDR regions.

The specification also clearly provides the sequences for all six CDR regions of the antibody 1G4. The full variable region sequences for the heavy and light chains of antibody 1G4 are shown in Figures 4a and 4b as SEQ ID NOs: 10 and 18, respectively. SEQ ID NOs: 10 and 18 necessarily contain all six of the CDR regions of antibody 1G4. In addition, the specification specifically calls out the heavy and light chain CDR3 regions of antibody 1G4 as separate sequences, e.g., SEQ ID NOs: 45 and 49, respectively (see e.g., paragraph [0038] of the published application).

Furthermore, at the time the application was filed, it was well within the purview of the ordinarily skilled artisan to determine the position of the remaining CDRs within the heavy and light chain variable region sequences provided in the specification, e.g., CDRs 1 and 2 located within the light chain variable region of SEQ ID NO: 10 and CDRs 1 and 2 located within the heavy chain variable region of SEQ ID NO: 18. In particular, since at least as early as 1991, the framework and CDR sequences of an antibody could be unambiguously determined and assigned using the Kabat numbering system. *See*, e.g., Kabat *et al.* (1991) "Sequences of Proteins of Immunological Interest." NIH Publication No. 91-3242, U.S. Department of Health and Human Services, Bethesda, MD ("Kabat *et al.*" cited in the Office Action Responses of December 29, 2009 and April 22, 2010). In particular, the Kabat *et al.* numbering system is a widely established method for assigning amino acid residues of an immunoglobulin molecule to a particular domain, such as a framework region (FR) or CDR. Specifically, Kabat *et al.* aligns 324 mouse kappa light chain group V sequences and 262 mouse heavy chain subgroup I(A) sequences and delineates each FR and CDR region for the heavy and light chains. *Supra* at pages 208-223 and 339-350. The alignments clearly show the delineation between the CDR regions and the FR regions of the antibodies, i.e., the CDRs are regions of high sequence variability interspersed between the well conserved framework regions.

Based on the teachings of Kabat *et al.*, one of ordinary skill in the art could readily identify the framework regions in any antibody, including the 1G4 antibody of the instant disclosure. For

example, a comparison of the first-listed Kabat *et al.* heavy chain sequence on page 339 with the heavy chain sequence of antibody 1G4 (SEQ ID NO: 18) is shown below:

```
...-FR1-- -CDR1- -----FR2------ ------CDR2------ -FR3-....KABAT (PAGE 339)
...TGDSIT        WIRKFPGNKLEYMG                  RISIT    KABAT (PAGE 339)
...TGYSIT SGYYWN WIRQSPGNKLEWMG YISTDGNSDYNPSFKN RISIT....SEQ ID NO: 18
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As shown in the alignment above, the borders of the FR regions as taught by Kabat *et al.* directly correspond to the borders of the framework regions of SEQ ID NO: 18. Therefore, it is readily apparent where regions FR1, CDR1, FR2, CDR2 and FR3 fall within SEQ ID NO: 18. Accordingly, the identities of the heavy chain CDR regions for antibody 1G4 were clearly taught in the instant application by disclosing SEQ ID NO: 18.

Furthermore, CDRs 1 and 2 of the variable region of antibody 1G4 (e.g., within SEQ ID NO: 10) are similarly readily identifiable using the Kabat *et al.* numbering system. In addition, Kabat *et al.* specifically teach in Table 1 (page xvi) that CDR1 of the light chain corresponds to residues 24-34 of the variable region and CDR2 of the light chain corresponds to residues 50-56 of the variable region. These are the specific residues of SEQ ID NO: 10 claimed in the instant application with respect to CDRs 1 and 2 of the light chain of antibody 1G4. Accordingly, the identities of the light chain CDR regions for antibody 1G4 were clearly taught in the instant application by disclosing SEQ ID NO: 10.

Furthermore, Applicants submit that it is permissible to refer to features inherently disclosed in an application without introducing new matter. In particular, MPEP 2163.07(a) states:

> By disclosing in a patent application a device that inherently performs a function or has a property, operates according to a theory or has an advantage, a patent application necessarily discloses that function, theory or advantage, even though it says nothing explicit concerning it. The application may later be amended to recite the function, theory or advantage without introducing prohibited new matter. *In re Reynolds*, 443 F.2d 384, 170 USPQ 94 (CCPA 1971); *In re Smythe*, 480 F. 2d 1376, 178 USPQ 279 (CCPA 1973) (Emphasis added).

As the light chain CDR3 and the heavy chain CDR3 of antibody 1G4 (SEQ ID NOs: 45 and 49) represent the Kabat CDR sequences, Applicants clearly defined the CDRs according to the method of Kabat *et al*. In addition, the instant specification clearly defines all six CDRs of a variety of other antibodies in Figure 4c using the method of Kabat *et al*. Accordingly, one of ordinary skill in the art would have understood that disclosure of the 1G4 light chain (SEQ ID NO: 10) and heavy chain (SEQ ID NO: 18) were disclosures of the Kabat *et al*. defined CDRs that fall within these sequences. Accordingly, no new matter was introduced by specifically referencing these CDRs in the claims because they are inherent features of the 1G4 antibody sequence.

In view of the above, Applicants submit that one of skill in the art would have understood that the application clearly supports the pending claims and that Applicants were in possession of the claimed invention. Withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicants believe the pending application is in condition for allowance. The Examiner is invited to telephone the undersigned to discuss any issue pertaining to this response. Applicants request favorable consideration of the application and early allowance of the pending claims.

Applicants believe no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. ALEX-P01-112 from which the undersigned is authorized to draw.

Dated: June 17, 2010

Respectfully submitted,

By: /Ryan Murphey/

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